EVIDENCE ON DEVELOPMENTAL AND REPRODUCTIVE TOXICITY OF SODIUM NITRITE

Reproductive and Cancer Hazard Assessment Section (RCHAS)
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Epidemiologic studies

- Childhood leukemia
- Childhood brain tumors

Epidemiologic approach

- Dietary intake during pregnancy as recalled by mothers
- Exposure: frequency of consumption of cured meats
- Controls matched on date of birth, race; identified by random digit dialing
- Adjustment in analyses for other factors (e.g., SES, other exposures, maternal age)

Childhood Leukemia and Maternal Diet During Pregnancy

Study characteristics

- Three case-control studies
- Two smaller studies, one large (232 cases)
- Various ages (<1 year, 0-14, 1-10)
- Leukemia types mixed or separated
- Largest study had detailed exposure information

Childhood Leukemia and Maternal Diet During Pregnancy

Maternal consumption of cured meats

- No statistically significant increased risks
- Possible dose-response effect observed for hot dogs in large study ($p \leq 0.1$)
- Apparent difference in risk by leukemia type in study of infants

Childhood Leukemia: Other Relevant Data

Childhood consumption of cured meats

- Largest study:
  Dose-related trend for hot dogs ($p \leq 0.001$)
  Significant OR=5.8 in high dose group
- Infant study: No data
- Study of one leukemia type (ALL):
  Significant risk associated with hot dog consumption in those who took no vitamins

Childhood Brain Tumors and Maternal Diet During Pregnancy

Study characteristics

- Nine case-control studies of brain tumors
- Published in 1982 - 1996
- U.S. and Canada, France and Australia
- Cases identified through cancer registries
- Age at diagnosis: 0 - 14 or 15 years (6 studies); 0-6 (2 studies), 0-19 (1 study)
- Largest study had 540 cases (801 controls)

Childhood Brain Tumors and Maternal Diet During Pregnancy

<u>All cured meats</u>

- Statistically significant increased risks in four studies & one published abstract
- ORs ranging from 1.4 to 2.5
- Dose-response effect observed in largest study

Childhood Brain Tumors and Maternal Diet During Pregnancy

<u>Hot dog consumption</u>

- Statistically significant increased risks in four of six studies
- ORs ranging from 1.4 to 2.3
- Possible dose-response effect observed in one large study reported only in abstract form

Childhood Brain Tumors: Maternal Vitamin Use

- Prenatal vitamin use decreased risk when used throughout pregnancy
  OR=0.54, $p<0.05$
- Prenatal vitamin use reduced risk associated with cured meat consumption
  Median intake of cured meat
  OR=2.4, $p<0.05$ without vitamins
  OR=1.3 $p=0.05$ with vitamins

Childhood Brain Tumors: Other Relevant Data

- Childhood consumption of cured meats: four studies with mixed results
- Seven of 10 published case-control studies of adult brain tumor risk found an association with cured meat intake

Additional Considerations

- Potential for biased recall of diet
- Association with food group could be proxy for another exposure (e.g., fat)
- Sodium nitrite exposure levels not quantified
- Effect examined in a variety of populations
- Relatively consistent effect across a range of studies of childhood brain tumors